REMARKS

Claims 1-9 are pending. The specification has been amended at page 2 to correct an obvious error in the structure depicted for the Nolan's catalyst. The structure for this catalyst should contain a double bond in the imidazoline ring, as is clearly shown by the structure at page 21 of the WO 00/59929 reference of record in this application. Since this amendment therefore corrects an obvious error in the application as filed, there is now new matter being introduced and entry of the amendment is requested.

Claims 1-9 stand rejected under 35 USC 103(a) as being unpatentable over WO 00/59929 in view of Grela et al. (*Angew.Chem. Int. Ed.* (2002), 41, No. 21, pgs 4038-4040). The Examiner argues that WO 00/59929 teaches the claimed ring-closing metathesis reaction in the presence of ruthenium-based catalyst such Grubb's and Hoveyda's catalysts, but does not teach using the ruthenium catalyst of compound IV of the instant claims. The Examiner then turns to Grela as teaching the use of the ruthenium catalyst of compound IV for such ring-closing metathesis reactions. The Examiner argues that Grela teaches that this catalyst is improved as compared to Hoveyda's catalyst, with improved efficiency of reaction, ease of obtaining the catalyst, can be operated under mild conditions and broad application in metathesis reactions applicable to the instant application, and therefore it would have been prima facie obvious to use such catalyst for the process disclosed in WO 00/59929 and arrive at the present invention.

Applicants respectfully traverse.

Without conceding that the Examiner has presented a prima facie case of obviousness, Applicants respectfully submit that they are in possession of comparative evidence that demonstrates the unexpectedly improved results obtained with a catalyst of formula IV as compared to both the Hoveyda's and Grubb's catalysts employed in WO 00/59929. Such comparative evidence will be described in detail further below. Applicants submit that the unexpected results obtained with the present invention are secondary considerations that rebuts any prima facie case of obviousness that may have been established.

In particular, reference is made to the experimental results presented in the Appendices attached to the present Amendment, which Appendices are summarized below:

Appendix 1: Details the metathesis reaction and catalysts that were tested in the experimentation.

Appendices 2A and 2B: Details the results of a comparison between the Grela and Hoveyda I catalysts for the conversion of 2b to 1. When using the Hoveyda I catalyst (test 2), 1 mol% of catalyst was added at the beginning and after 60 minutes and 120 minutes for a total of 3 mol% catalyst. When using the Grela catalyst (test 1), 0.4 mol% of catalyst was added at the beginning and 0.2 mol% after 60 minutes for a total of 0.6 mol% catalyst. Results were determined via HPLC-area%. It is demonstrated that a higher yield can be obtained with the Grela catalyst even with less amount of catalyst (a total of 0.6 mol% compared to 3 mol%), less addition steps (2 additions) and in significant shorter time periods.

Appendices 3A and 3B: Details the results of a comparison between the Grela, Hoveyda I and Grubbs catalysts for the conversion of 2b to 1. In this process, 2b was added to toluene and the solution was then added over 1 hour continuously to a solution of 0.7 mol% catalyst in toluene. Results were determined via HPLC-area%. This test further demonstrates the higher yields and higher reaction speeds obtainable when using the Grela catalyst.

Applicants respectfully submit that a careful analysis of these results and the teachings set forth in the cited Grela reference will indicate that such results are unexpected even in light of the teachings in Grela. First, the only experimental data in the Grela reference that appears to be relevant at all to the process of the present invention are Entries 3 and 4 in Table 1 at pg. 4039, which show either the same or lower activity for the Grela catalyst as compared to the referenced Grubbs catalyst 1b when conducting ring-closing metathesis reactions to prepare cyclic disubstituted olefins. Entries 3 and 4 of Grela show no improvement over a Grubbs-type catalyst. See particularly Entry 4 which shows lower yields even with higher catalyst loading and longer reaction time. Note that both Entries 1 and 5 in Table 1 are directed to the preparation of cyclic trisubstituted olefins (eg, compound 11a), and Entry 2 is directed to an en-yne type reaction, both of which processes are distinct from the RCM process of the present invention and, therefore, of less relevance to the present invention. Furthermore, all

the molecules set forth in Grela are of a relatively simple structure as compare to the large and highly functionalized structures of the diene compounds reacted according to the present invention, such as formula III and compound 2b.

For the reasons set forth above, Applicants submit that it would not have been expected that the specific RCM reaction of the present invention would be faster and more efficient based merely on the teachings set forth in the Grela reference. In view of these unexpected results, Applicants respectfully submit that the present invention as a whole is non-obvious over the cited art and withdrawal of this rejection is therefore requested.

In view of the above amendments and remarks, Applicants respectfully submit that this application is now in condition for allowance and earnestly request such action. If any points remain at issue which can best be resolved by way of a telephonic or personal interview, the Examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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